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ALTITUDE ACCLIMATIZATION AND BLOOD VOLUME: EFFECTS OF EXOGENOUS ERYTHROCYTE VOLUME EXPANSION

BY

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ABSTRACT

We studied sea-level residents during 13 days of altitude acclimatization to determine: (a) altitude acclimatization effects on erythrocyte volume and plasma volume; (b) if exogenous erythrocyte volume expansion alters subsequent erythrocyte volume and plasma volume adaptations; (c) if an increased blood oxygen content alters erythropoietin responses during altitude acclimatization; and (d) mechanisms responsible for plasma loss at altitude. Sixteen healthy men had a series of hematologic measurements made at sea level, on the first and ninth day of altitude (4,300 m) residence and after returning to sea level. Twenty-four hours before ascent to altitude, one group received a 700 ml infusion of autologous erythrocytes (42% hematocrit), while the other group received only a saline infusion. Erythrocyte infusion increased erythrocyte volume by ~10% while saline infusion had no effect; in addition, initially at altitude blood oxygen content was 8% higher in erythrocyte infused than saline infused subjects. The new findings regarding altitude acclimatization are summarized: (a) erythrocyte volume does not change during the first 13 days and is not affected by prior exogenous expansion; (b) a modest increase in blood oxygen content does not modify erythropoietin responses; (c) plasma losses are related to vascular protein losses; and (d) exogenous erythrocyte volume expansion coincides with transient increases in plasma loss, vascular protein loss and mean arterial pressure elevation. These findings better define human blood volume responses during altitude acclimatization.

Key Words: erythropoietin; hypoxia; mean arterial pressure; plasma protein; plasma volume

INTRODUCTION

Persons acclimatized to high terrestrial altitudes have elevated hemoglobin concentration which helps maintain oxygen delivery to tissues (7,45). Depending upon the altitude and duration of acclimatization, the hemoglobin elevations will be associated with either a decrease, no change, or increase in blood volume compared to sea-level values (24). The reason for disparate blood volume responses is because hemoglobin elevations are mediated by plasma loss (hemoconcentration), erythrocyte volume expansion or both (7,45). After ascent to altitude, a rapid (hours) plasma loss occurs (9) which is followed by a gradual erythrocyte volume expansion (28,39). The plasma loss has been attributed to dehydration, diuresis, plasma protein loss and increased capillary hydrostatic pressures (9,12,40), however, the exact mechanism(s) and transcapillary forces responsible are poorly understood. Erythrocyte volume expansion is mediated by erythropoietin which causes reticulocytes to appear within several days (5), however, the time course and magnitude of erythrocyte volume adaptations during altitude acclimatization is not well documented or understood (41).

Previous studies examining erythrocyte volume adaptations in the same subject before and after altitude acclimatization have all employed methodologies (carbon monoxide rebreathing and labeled albumin) that measure a volume of distribution potentially confounded by physiologic reactions (e.g., increased myoglobin concentration and vascular permeability to protein) to altitude (1,14,20,35,36,42). Recently, two of those studies (35,42) reported a large (~0.5 L) erythrocyte volume expansion in less than 3-wks of altitude acclimatization, while the earlier studies (1,14,20,36) reported no expansion with acclimatization to similar altitudes and

durations. These large erythrocyte expansions are in excess of maximal changes that might be reasonably expected (see discussion). Erythrocyte volume adaptations during short-term altitude acclimatization need to be investigated with methodologies which are not confounded by other physiologic reactions to altitude.

Ascent to altitude induces rapid increases in plasma erythropoietin with peak concentrations after ~48 h, followed by a decline toward baseline concentrations during 5-10 days of altitude acclimatization (6,8). The secondary decline in plasma erythropoietin concentration has been suggested to be mediated via increasing blood oxygen content, increasing arterial oxygen partial pressure and increasing alkalosis which all occur during altitude acclimatization (4,8,18). In an animal study, an abrupt large increase in blood oxygen content suppressed erythropoietin production (4). No human study has examined the effects of increased blood oxygen content on erythropoietin responses during altitude acclimatization.

The specific purposes of this study were to determine: (a) altitude acclimatization effects on erythrocyte volume and plasma volume; (b) if exogenous erythrocyte volume expansion alters subsequent erythrocyte volume and plasma volume adaptations; (c) if an increased blood oxygen content alters erythropoietin responses during altitude acclimatization; and (d) mechanisms responsible for plasma loss at altitude. We hypothesized that 13-days of altitude acclimatization would induce a small erythrocyte volume expansion, that increased blood oxygen content would depress plasma erythropoietin responses at altitude and suppress erythrocyte volume expansion, and that plasma loss would be associated with protein loss and elevated blood pressure at altitude. Also, this study is the first to examine the effects of altitude acclimatization on

erythrocyte volume using a methodology that measures a volume of distribution which is not confounded by effects of altitude acclimatization. These experiments were part of a larger study regarding erythrocyte infusion and exercise performance at altitude, and other procedures are being reported separately (43). The erythrocyte reinfusion experiments provided an excellent opportunity to address these important hematologic issues regarding altitude acclimatization.

METHODS

Subjects. Sixteen healthy male Caucasians from a US Army Special Forces Group stationed at Fort Devens, MA gave voluntary and informed consent to participate in this investigation, which was approved by the appropriate institutional review boards. Investigators adhered to AR 70-25 and the US Army Research and Materiel Command Regulations 70-25 on Use of Volunteers in Research. The subjects were divided into an erythrocyte reinfusion (ER) and saline infusion (CON) group (n=8 each) that were matched for age (30± 3 yr), weight (83± 8 kg) and maximal aerobic power (53± 4 ml/kg/min).

Protocol. During the late winter and spring, two units of blood were removed by phlebotomy (spaced by five weeks) and stored by the glycerol freezing method (38). Blood was separated into erythrocyte and plasma components; the erythrocytes were frozen in 40% (wt/vol) glycerol solution and stored at -80 degrees C. Eight weeks separated the last phlebotomy and any testing. About 2 weeks before infusion, the subjects' total body water, blood volume, arterial blood gases and blood pressure were measured. After completing sea-level testing, the ER group received ~700 ml of sodium-glucose-phosphate solution containing a ~42% hematocrit

(autologous erythrocytes), while the CON group received ~700 ml of the sodium-glucose-phosphate solution only. Twenty-four hours post-infusion, the subjects' blood volumes were again measured and they were then transported, via commercial air and automobile, to altitude. They arrived at altitude (Pikes Peak, CO; 4,300 m) about 8 h after leaving sea level (Boston, MA).

Subjects lived on the summit of Pikes Peak (John T. Maher Memorial Laboratory) for the next two weeks, while completing additional testing and engaging in military mountaineering training. Military mountaineering training included lectures mixed with intermittent strenuous activity including rock climbing, repelling, rescue techniques and hiking. During their stay on Pikes Peak considerable efforts were made to provide an adequate caloric and fluid intake to offset the anorexia often experienced at altitude. In addition, standardized diets were employed during the 24 h preceding body fluid and hematologic measurements at altitude. Total body water, hematologic and blood pressure measurements were repeated on days one (HA1; 10-14 h post arrival) and nine (HA9) of altitude residence. On the thirteenth day at altitude, subjects were transported back to sea level (Boston). Blood volumes were measured immediately upon arrival (~8 h after leaving Pikes Peak) to sea level.

Procedures. Throughout the study, any set of measurements was conducted at the same time of day. Blood pressure was measured by auscultation and mean arterial pressure (MAP) was calculated. Total body water was measured as the volume of dilution of deuterium-labeled water in the body (32). On days when blood volume and total body water were measured the subjects were in a post-absorptive state. Erythrocyte and plasma volumes were measured by the

radioactively labeled chromium (^{51}Cr) and iodine (^{125}I) albumin methods, respectively (31). Blood samples were obtained prior to and 10 min and 20 min following the infusion of autologous ^{51}Cr labeled erythrocytes and ^{125}I-albumin. The mean radioactivity in the blood from these samples was used to determine the vascular volumes and no extrapolation was made to time zero. In our laboratory, this methodology has demonstrated maximal differences of 5% for erythrocyte volume and 3% for plasma volume between repeated measurements over a seven day period (unpublished data). Overall hematocrit was calculated as the ratio of measured erythrocyte volume to the sum of measured erythrocyte volume and measured plasma volume. The F-cell ratio was calculated from the ratio of overall hematocrit to the peripheral venous hematocrit (not corrected for trapped plasma).

Before the subjects ascended to altitude both erythrocyte and plasma volumes were measured twice: pre- (SL1) and again post- (SL2) erythrocyte or saline infusion. On the day subjects returned to sea level both erythrocyte volume and plasma volume were measured a third time (SL3). The plasma volumes for HA1 and HA9 were calculated from the measured erythrocyte volumes obtained immediately before going to (SL2) or returning (SL3) from altitude, and appropriate hematocrit data (HA1 or HA9). For these calculations, we assumed that erythrocyte volumes remained constant during the ~24 hrs between SL2 and HA1 and the five days between HA9 and SL3. Erythrocyte volumes were corrected for the amount of erythrocytes removed. Plasma volumes were not corrected for overall to peripheral hematocrit differences. Blood volumes were calculated as the sum of erythrocyte volume and plasma volume values.

Whole blood was analyzed for hematocrit (micro-centrification), hemoglobin, oxygen

content, oxygen partial pressure (P_aO_2), pH_a, and in vitro hemoglobin O_2 half-saturation pressure (P_{50}). Arterial blood gases were analyzed via an automated system (Radiometer ABL blood gas analyzer). Plasma was analyzed for protein concentration (American Optical Refractometer) and erythropoietin concentration (EIA Kit Quantikine IVD; R&D Systems, Minneapolis MN). Total circulating protein was calculated as the product of plasma protein concentration and plasma volume. Arterial blood was collected from a radial artery catheter in heparinized gas impermeable glass syringes, that were immediately capped and chilled after blood collection. Venous blood was obtained from an indwelling catheter within a superficial forearm vein, however, occasionally venipunctures were employed. Appropriate controls for body posture and arm position were employed prior to blood collections (29).

Statistics. All values are reported as means and standard deviations unless otherwise noted. Analyses of Variance for Repeated Measures (subject X treatment X day) were used to test for interaction and main effects. Significant effects were localized by post hoc testing using Neuman-Kuels procedures. In addition, Student's t test for independent samples was employed were appropriate. Pearson product moment correlations were performed to examine relationships between selected variables. Statistical significance was tested at the $P<0.05$ level. A computerized statistical package (CSS:STAT-ISTICA, Statsoft Corp.) was used for data analyses.

RESULTS

Infusion Effects

The ER group received 0.29± 0.18 L of erythrocytes which increased (P<0.05) their erythrocyte volume by 0.27± 0.17 L or 10% and corresponded to a ~95% survival rate. After erythrocyte infusion, plasma volume decreased (P<0.05; 0.25± 0.25 L) and blood volume remained unchanged. Erythrocyte infusion increased (P<0.05) oxygen content (20.2± 1.2 to 21.2± 1.5 ml O_2/100 ml) with no change in P_{50} (29.5± 3.9 mmHg). The CON group had no change in erythrocyte volume, plasma volume, blood volume, oxygen content (19.8± 0.8 ml O_2 /100 ml) or P_{50} (27.9±2.5 mmHg).

Altitude Effects

While living in Pikes Peak eating and drinking was emphasized, and diet was standardized for 24 h prior to SL2, HA1 and HA9 measurements. For 24 h prior to those trials, the average total caloric intake was 2,723 Kcal, sodium intake was 72 mEq and total fluid (food & drink) intake was 5.8 L. Body weight decreased (P<0.05) by 1.3 kg from HA1 to HA9, and there were no group differences. Total body water (SL=52.4±1.3 L; HA1=51.6±1.0 L; (HA9=51.7±1.0 L) did not change at altitude and there were no group differences. Hematocrit increased (P<0.05) from SL1 (ER= 40.0±1.8 %; CON= 39.7± 1.0 %) to HA1 (ER= 45.4±2.5 %; CON= 41.3± 0.9 %) and HA9 (ER= 44.0±1.0 %; CON= 42.2±0.7 %), and was greater (P<0.05) for ER at HA1 and HA9.

Figure 1 provides the erythrocyte volumes, plasma volumes and blood volumes at sea level and altitude. Erythrocyte volume did not change at altitude and there were no group differences. Plasma volume decreased (P<0.05) at altitude, with greater (P<0.05) plasma loss for ER (0.72± 0.46 L) than CON (0.31±0.34 L) at HA1 but not at HA9. Blood volume decreased

($P<0.05$) at altitude and there were no group differences. F-cell ratio was 0.89± 0.04 at SL2 and 0.88± 0.04 at SL3 with no group differences.

Figure 2A (left panel) presents individual data for protein concentration differences and plasma loss from sea level to altitude. Plasma protein concentration differences remained constant with marked plasma loss at altitude. Total circulating protein (TCP) decreased ($P<0.05$) at altitude for ER (SL2=258± 37 g; HA1=224±56 g; HA9=235± 67 g) and CON (SL2= 277±28 g; HA1=257±40 g; HA9=268±31 g), with a greater reduction ($P<0.05$) at HA1 for ER than CON. Strong relationships were found between TCP loss and plasma loss at HA1 ($P<0.05$; $r=0.87$) and HA9 ($P<0.05$; $r=0.93$). Figure 2B (right panel) presents individual changes in TCP and plasma loss from sea level to altitude, the line represents a theoretical relationship between these variables if only transcapillary oncotic forces were responsible. For each subject, the relationship between protein loss and plasma loss at altitude was close to the theoretical relationship.

FIGURE 1 AND FIGURE 2 ABOUT HERE

Figure 3 presents EPO concentrations at sea level and altitude. EPO concentration increased ($P<0.05$) from SL1 to HA1 and then declined ($P<0.05$) to baseline values at HA9 and SL3 with no group differences. Oxygen content, P_aO_2 and pH_a values have been reported elsewhere (44). In brief, oxygen content decreased ($P<0.05$) from SL1 to HA1 and HA9, and ER had higher ($P<0.05$) values than CON at HA1 (18.2±1.9 vs 16.8±1.5 ml O_2/100 ml). P_aO_2 values decreased ($P<0.05$) from SL1 to HA1 and HA9 with no group differences. pH_a values increased ($P<0.05$) from SL1 to HA1 and HA9 with no group differences. No relationships were found change in EPO concentration and change in oxygen content, P_aO_2, pH_a values from SL1 to HA1

and from SL1 to HA9.

FIGURES 3 ABOUT HERE

Systolic blood pressure was similar at SL1 (119± 7 mmHg) and HA1 (122± 3 mmHg), but increased ($P<0.05$) from SL1 to HA9 (128± 7 mmHg) with no group differences. Diastolic blood pressure was the same at SL1 (76± 9 mmHg) and HA1 (79± 12 mmHg) , but increased ($P<0.05$) from HA1 to HA9 (92± 5 mmHg) and from SL to HA9 with no group differences. MAP increased ($P<0.05$) from SL1 values (90± 7 mmHg) at altitude, and values were greater at HA1 for ER than CON ($P<0.05$; 98±9 vs 89±7 mmHg) but not at HA9 (104±4 mmHg). There was no significant relationship between increased MAP and plasma loss between SL1 with HA1 and HA9.

DISCUSSION

Our study was the first to examine the effects of altitude acclimatization on erythrocyte volume using a methodology that measures a volume of distribution which is not confounded by effects of altitude acclimatization. We measured erythrocyte volume using radioactively labeled erythrocyte methodology, the accepted gold standard, and values averaged 30 ml/kg which compares favorably to normative values (range 25 - 32 ml/kg) for healthy young adults (31). Surprisingly, only three studies have used radioactively labeled erythrocyte methodology to investigate the erythrocyte volume expansion associated with long-term living at altitude (10,28,39). Weil and colleagues (39) measured the erythrocyte volume of fifteen sea-level, nineteen moderate-altitude (1600 m; Denver, CO) and thirty-nine high-altitude (3100 m;

Leadville, CO) residents and reported average values of 27 ml/kg, 27 ml/kg and 32 ml/kg, respectively. Sanchez and colleagues (28) measured erythrocyte volume of seven sea-level and thirteen high-altitude (4,330 m; Cerro de Pasco, Peru) residents and reported average value of 28 ml/kg and 52 ml/kg, respectively. Hartley and colleagues (10) measured the erythrocyte volume of ten high-altitude residents at Leadville, CO (3,100 m) and again after they spent ten days at sea level and reported average values of 28 ml/kg and 25 ml/kg, respectively.

We found that erythrocyte volume did not increase during 13-days of acclimatization at 4,300 m, which agrees with some (1,14,20,36) but disagrees with other (35,42) studies. Wolfel and colleagues (42) reported an erythrocyte volume expansion of 20% (0.48 L; from ~ 33 ml/kg to 40 ml/kg) after 18-days at 4,300 m, while Stokke and colleagues (35) reported an erythrocyte volume expansion of 28% (0.52 L; from ~ 26 ml/kg to 33 ml/kg) after 20-days at a mean altitude of 4,100 m. All of these previous studies used methodologies that were potentially confounded by physiologic reactions to altitude acclimatization (1,14,20,35,36,42). Wolfel and colleagues (42) estimated erythrocyte volume via carbon monoxide rebreathing, and carbon monoxide has a volume of distribution to all iron-porphyrin molecules which is 2%- 20% greater than erythrocyte volume (31). Hypoxia has been reported to increase concentrations of muscle myoglobin (2) and liver cytochrome P-450 (15). Therefore, the apparent erythrocyte volume expansion after altitude acclimatization reported by Wolfel and colleagues (42) might represent a greater extravascular volume of distribution for carbon monoxide. Stokke and colleagues (35) calculated erythrocyte volume from plasma volume measured by labeled albumin infusion and hematocrit values obtained at sea level and 5,300 m. Hypoxia increases vascular permeability to

albumin (22,40), therefore the infused albumin's volume of distribution might have included extravascular space.

The question arises, what is the maximum erythrocyte volume expansion rate that might reasonably be expected during altitude acclimatization? Some indication can be obtained by examining studies that made erythrocyte volume measurements, using erythrocyte labeling methods, before and after either erythropoietin administration or aerobic training (3,25,44). Berglund and Ekblom (3) compared two doses of erythropoietin (20 & 40 U/kg S.c. @ 3X / wk for 6 wks) on erythrocyte volume expansion in healthy young adults. Both dosages expanded erythrocyte volume by rates of 50 ml/wk. Since the erythrocyte volume expansion rate was not dose dependent, it may represent the maximal rate for healthy young adults. With exercise training, healthy young adults exhibit a erythrocyte volume expansion rate ranging from 10 ml/wk (44) to 30 ml/wk (25). In comparison, the 182 and 187 ml/wk erythrocyte volume expansion rate reported by Wolfel et. al. (42) and Stokke et. al. (35) during altitude acclimatization seem high.

A parallel question is what magnitude of erythrocyte volume expansion might have occurred during 13 days at altitude and not been detected with our measurement resolution? EPO can stimulate the appearance of reticulocytes within several days (5), and EPO levels were elevated at altitude, therefore (if production exceeded apoptsosis) a small undetectable erythrocyte volume expansion probably occurred. Using the same methodology employed in this study, we have been able to detect erythrocyte expansions as small as ~100 ml (44). Therefore, it is possible that erythrocyte volume might have expanded at rates of 10 to 50 ml/wk, as

demonstrated in EPO and training studies (3,25,44) and not have been detected by our measurements. Erythrocyte volume expansions of the magnitudes reported by Wolfel et. al. (42) and Stokke et. al. (35) are well within our measurement resolution (30,44), and this supports our belief that their measurements were confounded by altitude acclimatization.

Plasma volume decreased from sea-level by ~11% and ~9% on HA1 and HA9, respectively. This magnitude of plasma loss is comparable to previous studies, however, considerable inter-study variability (range 7% to 28%) does exist (1,9,11,13,14,22,36,40,42). We believe our emphasis on nutritional intake minimized dehydration's effects and plasma loss for several reasons. First, TBW was stable during acclimatization as reported by other studies (9,22) that carefully controlled nutritional conditions. Second, body weight decreased by only 1.3 kg during acclimatization, and if this weight loss was from dehydration it would reduce plasma volume by only ~2% (29). We found no additional plasma loss from HA1 to HA9 which agrees with one study (9), but does not agree with several other studies (14,36,42) that reported additional plasma loss during altitude acclimatization. In the study most comparable to ours, Krzywicki et. al. (14) reported plasma loss of 11% and 28% after 4 days and 12 days at 4,300 m. They found that total body water did not change during the initial four days at altitude, but it decreased by 2.5 L between days 4 and 12 at altitude (14). Dehydration of this magnitude should account for about one-half (~6% reduction) of plasma loss between days 4 and 12 (29). Another factor which could contribute to the stable plasma volumes during altitude acclimatization was the relatively high physical activity levels performed by our subjects. Hoyt and Honig (12) have proposed that physical activity might help minimize the plasma loss associated with altitude

acclimatization.

We believe the plasma volume decrease at altitude was mediated by protein loss which reduced vascular oncotic pressure. For a given set of transcapillary hydrostatic and tissue pressures, a reduced plasma oncotic pressure with no change or increase of interstitial colloid osmotic pressure will cause less fluid to be held within the vascular space (29). Protein concentration differences remained constant with increasing plasma loss (Figure 2A) at altitude suggesting a proportionate loss between plasma oncotic pressure and fluid. In addition, a strong relationships between TCP losses and plasma losses, which approximates the theoretical relationship (Figure 2B) supports our belief. Previous investigators have reported TCP losses during altitude exposure (11,37,40), however, they have not quantitatively tied the protein loss to plasma loss. The TCP loss probably initially reflected increased capillary permeability to protein and later may have reflected increased degradation. Capillary permeability to albumin increases after several hours of hypoxia (22,33) and mediators may include elevated substance P, leukotriene B_4 and prostaglandin E_2 (21,27). Albumin degradation has been reported to occur within 8 days at altitude (37). An increased hydrostatic pressure probably did not contribute to plasma loss, as MAP increased while plasma loss remained constant during altitude acclimatization. An increased MAP has been associated with plasma loss during exercise at sea level and altitude (16,17).

For ER group there was greater plasma loss (0.72 vs 0.31 L), TCP loss (34 vs 20 g) and MAP elevations (8 vs 1 mmHg) at HA1. We are not aware of any mechanism(s) by which erythrocyte volume expansion would accentuate TCP loss. The greater MAP elevations might be

due to increased sympathetic activation and reduced hypoxia mediated vasodilation. Sympathetic activation changes during altitude exposure are not fully understood (26), but since between groups P_aO_2 was similar and blood oxygen content was higher it is doubtful that ER had greater sympathetic activation than CON. Another possibility is that reduced vasodilation was mediated by the increased erythrocyte volume and hemoglobin (total and concentration) acting as a nitric oxide scavenger (34). Nitric oxide is a potent smooth muscle relaxant (19), so greater hemoglobin could reduce nitric oxide concentrations at resistance vessels and increase MAP. Eventually the increased nitric oxide sink would become saturated so the vasodilator inhibition would be lost (e.g. HA9). If the smooth muscle relaxation was greater pre- than post-capillary this would increase capillary hydrostatic pressures to mediate net filtration and contribute to greater plasma loss (29).

Erythrocyte infusion had no effect on EPO responses at altitude. EPO concentrations achieved maximal levels at HA1, then decreased with altitude acclimatization and returned to baseline levels by SL3. These observations are consistent with previous research regarding EPO kinetics (6) and altitude acclimatization (8). Although mean EPO concentrations increased while mean P_aO_2 decreased, the individual changes in these parameters were not significantly correlated due to large inter-subject variability for EPO concentrations. For example, EPO concentration increases between SL1 and HA1 ranged from 5 to 56 mU / ml, and between SL1 and HA9 ranged from 0 to 28 mU / ml. These data indicate that the stimulus for EPO production during altitude exposure is probably more directly determined by factors such as renal oxygen delivery (23), rather than simply blood oxygen content or tensions. Bozzini and colleagues (4)

reported that a 37% blood oxygen content elevation suppressed EPO production in animals. In the present study, erythrocyte infusion induced an 8% higher oxygen content (ER vs CON) at HA1 and no differences in EPO responses were observed. If greater difference in oxygen content had been elicited perhaps different EPO responses might have been observed, however, such large (37%) elevations are not normally observed during altitude acclimatization.

In summary, our data indicate several new findings regarding 13 days of altitude acclimatization: (a) erythrocyte volume does not change during the first 13 days and is not effected by prior exogenous expansion; (b) a modest increase in blood oxygen content does not modify erythropoietin responses; (c) plasma losses are related to vascular protein losses; and (d) exogenous erythrocyte volume expansion coincides with transient increases in plasma loss, vascular protein loss and mean arterial pressure elevation. These findings help to define human blood volume and hematologic responses to altitude acclimatization.

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The view, opinions, and/or findings contained in this report are those of the authors and should not be construed as an official Department of the Army position, or decision, unless so designated by other official documentation. Approved for public release; distribution unlimited.

FIGURE LEGENDS

Figure 1. Erythrocyte volume, plasma volume and blood volume (mean ± standard error) of erythrocyte infused (ER) and control (CON) subjects at sea level and during altitude acclimatization.

Figure 2. (Left, A) Individual data for plasma protein concentration changes relative to plasma volume changes (altitude minus sea level). (Right, B) Individual data for changes in total circulating protein (TCP) and changes in plasma volume (PV) between sea level and the first (HA1) and ninth (HA9) days of altitude acclimatization for erythrocyte infused (ER) and control (CON) subjects. The line represents the theoretical relationship between these variables if only transcapillary oncotic forces were responsible for plasma loss (29).

Figure 3. Plasma erythropoietin (EPO) concentration (mean ± standard error) of erythrocyte infused (ER) and control (CON) subjects at sea level and during altitude acclimatization.

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Fig. 1 Sawka et al.

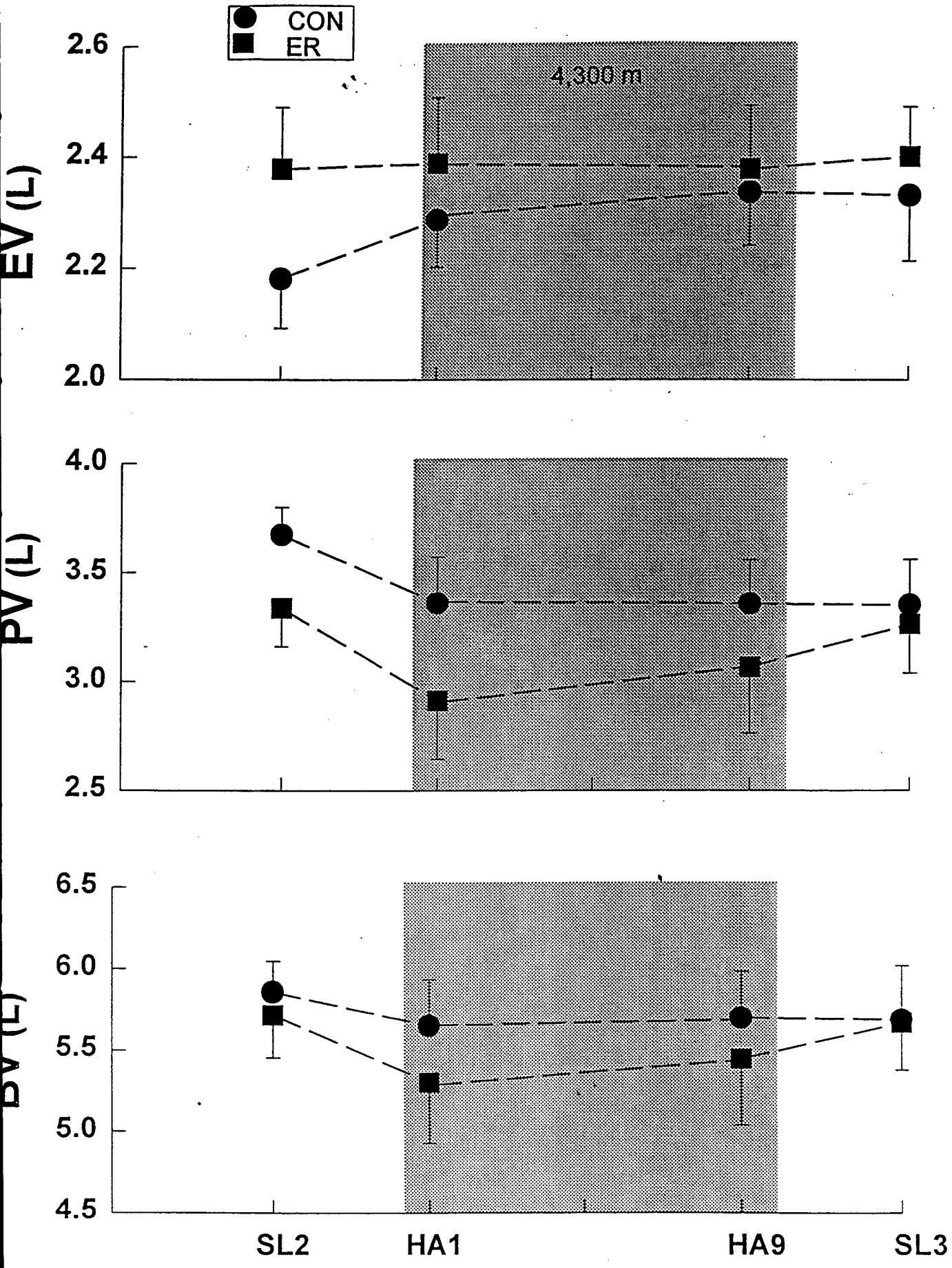
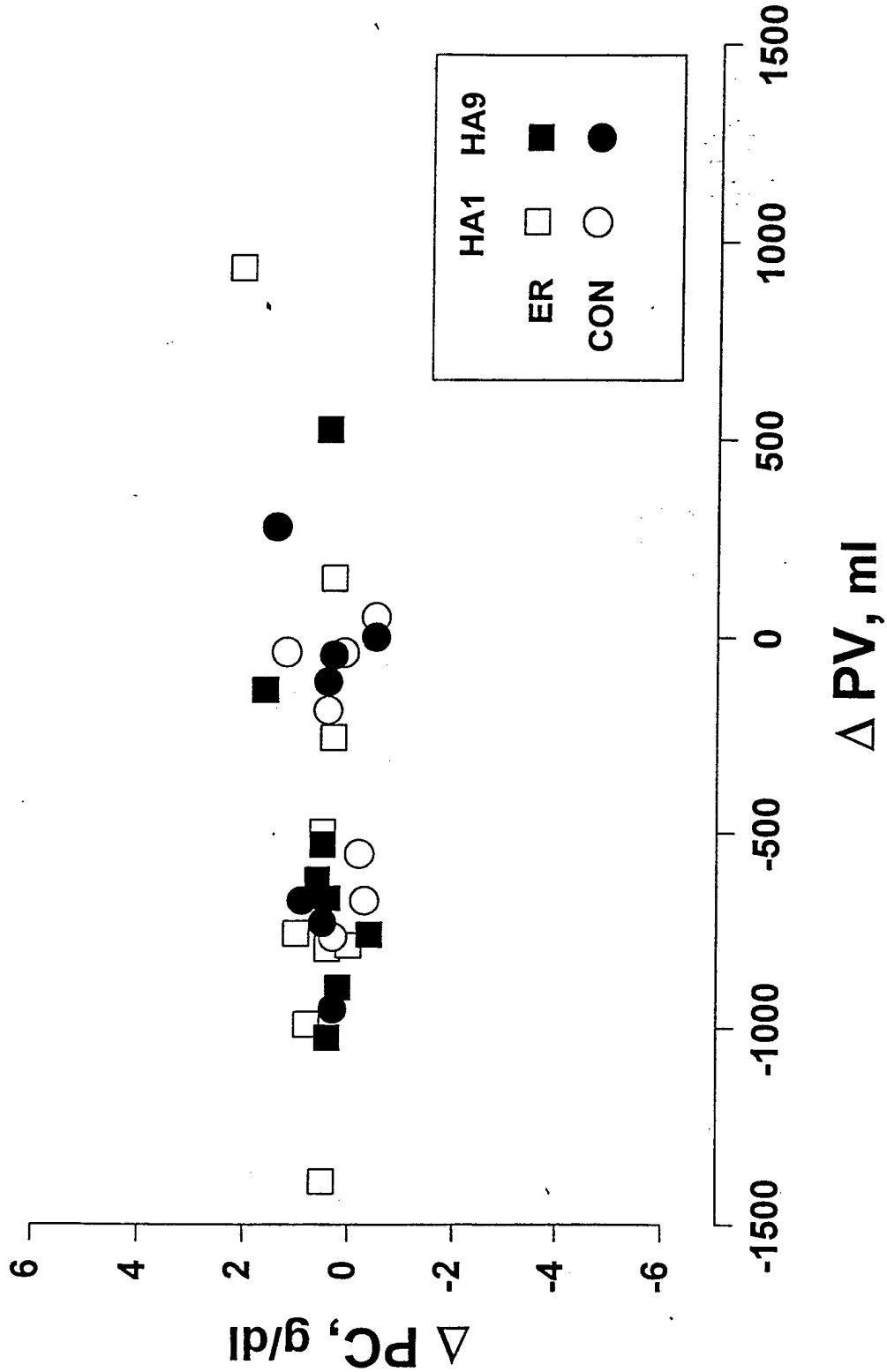
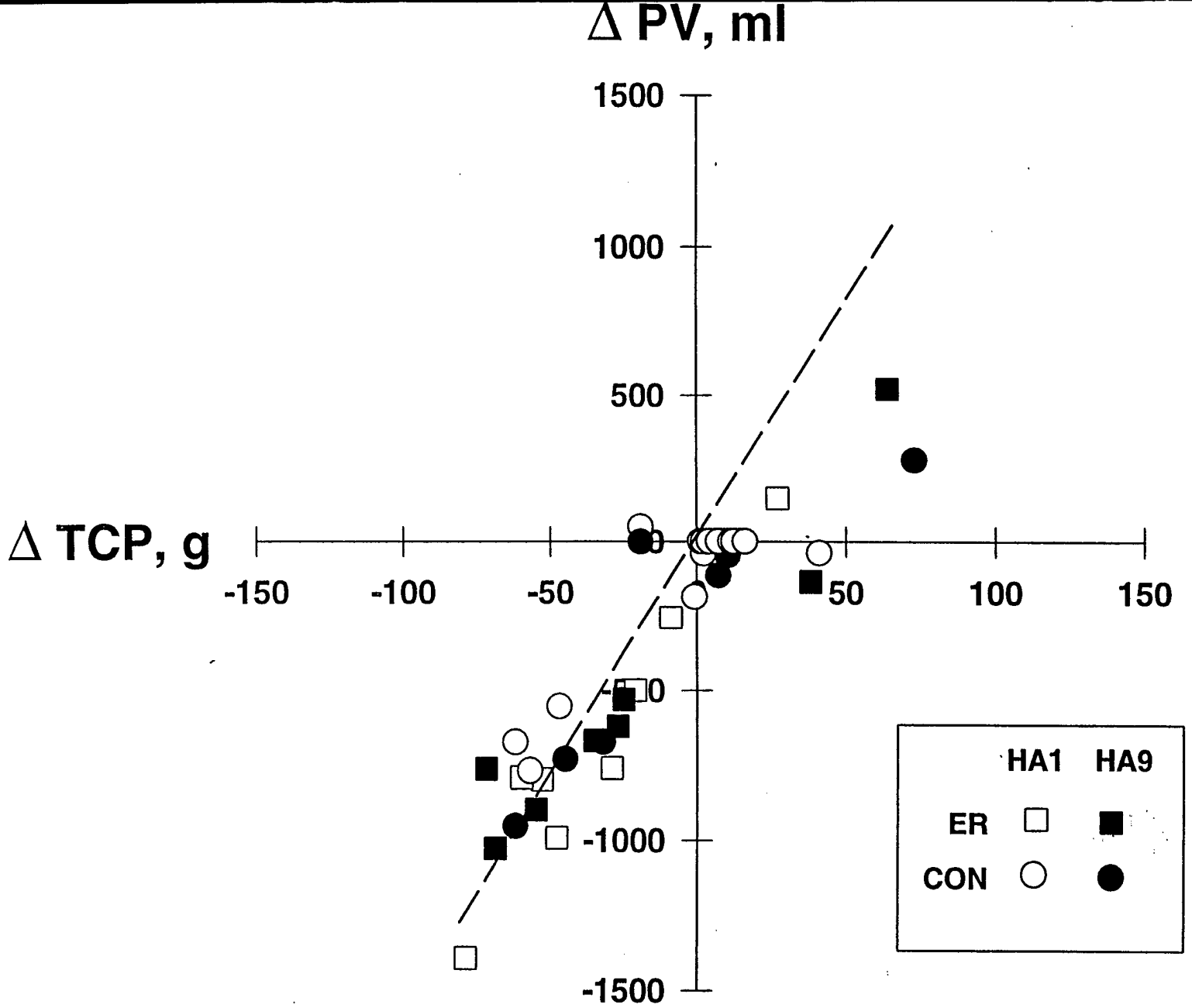


FIG. 6H SAWYER ET AL.




Δ PV, ml
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1000
500
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-1500
Δ TCP, g
-150
-100
-50
50
100
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HA1
HA9
ER
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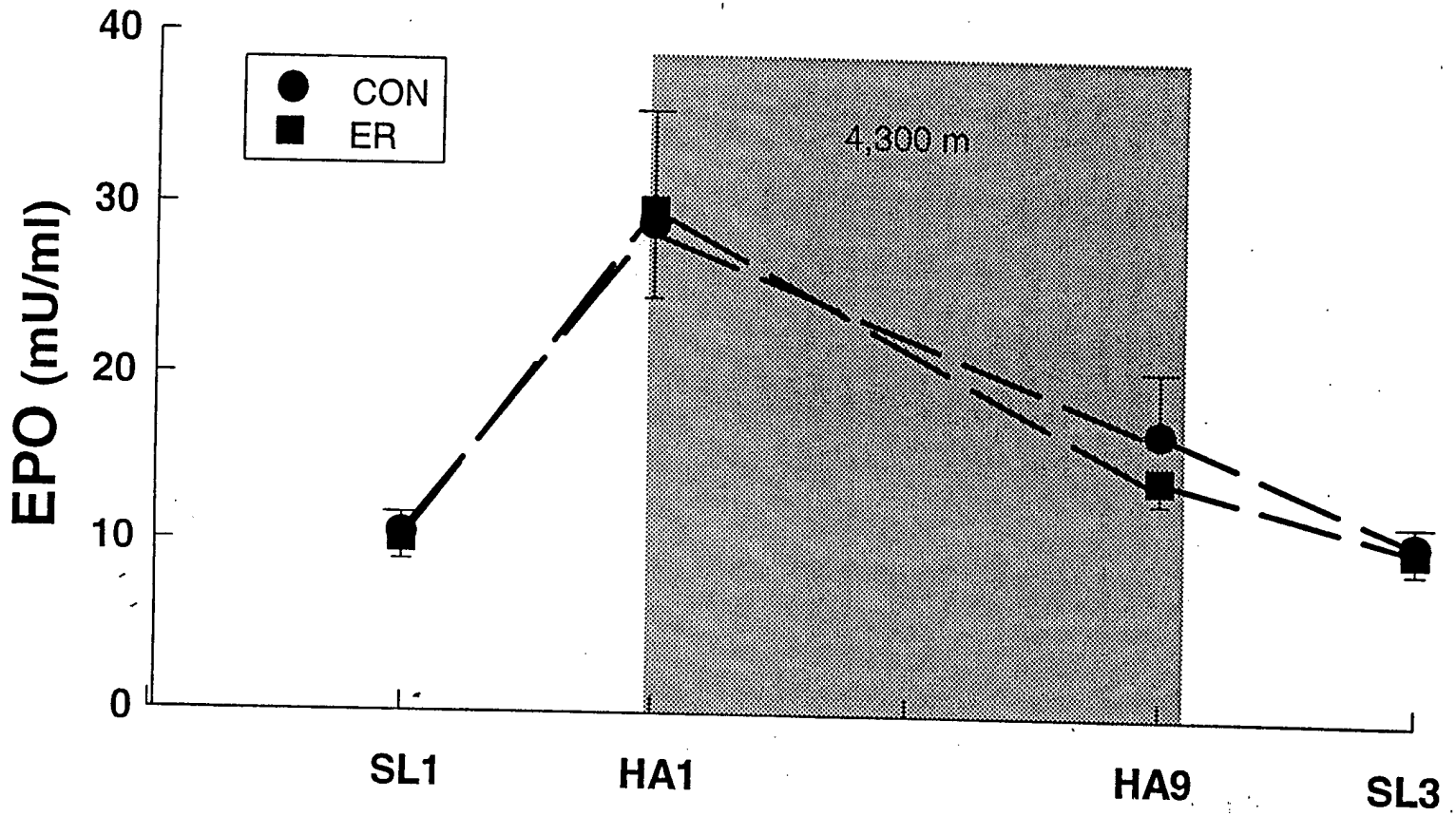
40
30
20
10
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EPO (mU/ml)
CON
ER
4,300 m
SL1
HA1
HA9
SL3